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Original article

Otorhinolaryngological findings in a group of patients with rheumatic diseases

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ABSTRACT

Introduction: Otorhinolaryngological manifestations of rheumatologic diseases represent a great challenge not only to the generalist physician but also to the ENT doctor and rheumatologist. They often represent early manifestations of an autoimmune disorder which requires prompt and aggressive immunosuppressive treatment. Auditory, nasal, laryngeal and eye symptoms can be the first manifestation of rheumatic diseases and their proper assessment helps the doctor to identify signs of disease activity. The objective of this study is to identify the ENT manifestations in patients with rheumatic diseases in a high complexity hospital, regarding facilitating an early diagnosis and treatment.

Methods: We performed clinical and complete otorhinolaryngological evaluations in patients selected from the outpatient rheumatology in a standardized manner by the use of a standardized form filling during the second half of 2010.

Results: In the study group, systemic lupus erythematosus (SLE) patients had predominantly laryngeal manifestations, while patients with Sjögren's syndrome showed a higher prevalence of otologic manifestations. Changes in audiometric tests were found in 53% of Wegener's granulomatosis (WG) patients, 80% of relapsing polychondritis (RP), 33% of systemic lupus erythematosus (SLE) and 50% of Churg-Strauss syndrome (SCS). Regarding nasal alterations, these were found so prevalent in all conditions, especially Churg-Strauss syndrome.

Discussion and conclusion: This study demonstrated that most patients treated in our hospital has the ENT signs and symptoms commonly associated in previous studies on rheumatic diseases, but further studies with a larger number of patients must be made to establish such relations.

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Achados otorrinolaringológicos em um grupo de pacientes com doenças reumatológicas

R E S U M O

Palavras-chave:

Reumatologia
Otorrinolaringologia
Doenças autoimunes

Introdução: As manifestações otorrinolaringológicas de doenças reumáticas representam um grande desafio não só ao médico generalista, mas também ao otorrinolaringologista e ao reumatologista. Frequentemente representam manifestações iniciais de uma desordem autoimune que exige um tratamento imunossupressor imediato e agressivo. Sintomas auditivos, nasais, laríngeos e oculares podem ser a primeira manifestação de doenças reumáticas, e sua correta avaliação auxilia o médico a identificar sinais de atividade da doença. O objetivo deste trabalho foi identificar as manifestações otorrinolaringológicas em pacientes com doenças reumáticas em um hospital de alta complexidade, no que se refere a facilitar diagnóstico e tratamento precoces.

Métodos: Foram realizadas avaliações clínicas e otorrinolaringológicas completas em pacientes selecionados no ambulatório de reumatologia, no segundo semestre do ano de 2010, de forma padronizada e com utilização de um formulário de preenchimento normatizado. **Resultados:** No grupo estudado, pacientes com LES apresentaram predominantemente manifestações laríngeas, enquanto pacientes com síndrome de Sjögren apresentaram predomínio das manifestações otológicas (100% dos casos). As alterações de exames audiométricos são encontradas em 53% dos casos portadores de GW, 80% de PR, 33% de LES e 50% de SCS. Quanto às alterações nasais, estas foram encontradas de forma prevalente em todas as patologias, principalmente a síndrome de Churg-Strauss.

Discussão e conclusão: Este estudo demonstrou que a maioria dos pacientes em seguimento em nosso serviço apresenta os sinais e sintomas otorrinolaringológicos comumente relacionados em trabalhos prévios sobre doenças reumáticas, porém novos estudos com um número maior de pacientes devem ser feitos para comprovar tais relações

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Introduction

Rheumatic diseases have a high prevalence rate worldwide and a representative functional disability index.¹ These conditions comprise a heterogeneous group of entities that produce systemic changes involving the connective tissue throughout the body. For this reason they may involve blood vessels and serous and mucous membranes of all the aerodigestive tract.² The treatment itself of such diseases with non-steroidal anti-inflammatory drugs can cause symptoms in many patients.³ In this sense, much has been discussed about the current ENT manifestations in patients with rheumatic diseases.⁴

Ear, nasal, laryngeal and ocular symptoms may be the first manifestations of various rheumatic diseases, as relapsing polychondritis (RP), systemic lupus erythematosus (SLE), Wegener's granulomatosis (WG), Sjögren's syndrome (SS) and Churg-Strauss syndrome (CSS),^{5,6} and this combination is described in several trials. As an example, there are some case reports of patients with RP in which changes in pinna, nasal cartilage, nasal septum, larynx and trachea were found, causing dysphonia, dyspnea and cosmetic deformities.^{7,8} Allergic rhinitis, chronic sinusitis and serous otitis media are commonly found in patients with CSS,⁹ while immunological abnormalities are frequently found in patients with Menière's disease.¹⁰ Sensorineural hearing loss may be the first manifestation of polyarteritis nodosa,¹¹ as

well as recurrent parotitis for SS¹² and chronic otitis media for ankylosing spondylitis.¹³

Given the global growth of rheumatic diseases, driven by population ageing and exposure to a larger number of inducers of autoimmune changes,¹⁴ the identification of ENT symptoms in these patients can become an important tool for the diagnosis and, consequently, for the early treatment of such diseases. The correct evaluation of rheumatic conditions, particularly in SLE, helps the physician to identify signs of disease activity, which directly affects the patients' quality of life and their prognosis.¹⁵⁻¹⁷

Thus, the objective of this work is to identify ENT manifestations in patients with rheumatic diseases in a hospital of high complexity. As this trial was conducted in 2010 and considering the fact that the old nomenclature for rheumatologic diseases is more widespread in our environment, we used this nomenclature in the present trial. In the new nomenclature established by the Chapel Hill Consensus in 2012, Wegener's granulomatosis became known as granulomatous with polyangiitis, and Churg-Strauss syndrome became known as eosinophilic granulomatous with polyangiitis.¹⁸

Materials e methods

In all patients, complete clinical and ENT evaluations consisting of a detailed history, a thorough ENT physical examination and audiometry, imitanciometry (acoustic impedance) and

nasofiberoendoscopia were performed. Sensorineural hearing loss or sound discrimination impairment with bilateral and symmetrical occurrence and with subacute evolution were considered as audiometric alterations.

The assessment was fully standardized, and a normatized filling form was used during the second half of 2010.

For the selection of patients, we requested from the Department of Rheumatology a random referral of patients for specialized ENT evaluation, but some specific outpatient services contributed more to the project (such as vasculitis and Wegener's granulomatosis outpatient services).

The first five patients in each outpatient rheumatology should have been referred for a period of 15 days.

Every patient evaluation was performed at the otorhinolaryngology ambulatory of our national reference, tertiary care, university hospital. The patients were attended and evaluated by two otolaryngologists randomly selected among the professionals who participated in this trial.

The criteria used were those of the Otorhinolaryngologist available at the time and who would perform the patient's assessment.

This trial was evaluated and approved by the Research Ethics Committee from our institution (Opinion CEP/FCM n° 1187/2011).

Results

Thirty-two selected patients of Rheumatology Discipline Outpatient Clinic (HC/FCM/UNICAMP) were evaluated. In the evaluated sample, the patients were diagnosed as defined by the criteria of Medical Guidelines of the Brazilian Society of Rheumatology¹⁹ for SLE and by the American College of Rheumatology^{20,21,22,23} for other diseases, with a diagnosis established for one from five rheumatic diseases: Wegener's granulomatosis (WG), Churg-Strauss syndrome (CSS), relapsing polychondritis (RP), Sjögren's syndrome (SS) and systemic lupus erythematosus (SLE).

The mean age of the participants was 41.7 years (range 22-70 years) and the mean disease duration was 9.12 years (range 1-40 years).

1 – Wegener's granulomatosis (n = 17)

Among WG patients, nine (53.1%) reported hearing loss and had low tone threshold results at audiometry. The most fre-

quent type of reduction was that of a bilateral sensorineural pattern, present in five patients (55.6%). In the context of rhinologic symptoms, nasal obstruction in 11 (64.8%) and rhinorrhea in ten (58.8%) patients were the most prevalent symptoms, with compatible changes present in the rhinoscopic exam in 12 (70.2%) of these patients, and the most frequent symptoms were coryza, septal perforations, mucosal oedema and turbinate hypertrophy. Complaints related to the larynx, dyspnea and raucousness were found in six (35.2%) and seven (41.2%) patients, respectively, being the most prevalent complaints. Of these, seven (41.2%) patients had an abnormal physical examination, for instance, hyperaemia of posterior pharynx, inter-arytenoidal oedema and relative degrees of subglottic stenosis (Table 1).

2 – Recidivant polychondritis (n = 5)

In patients with RP, among the otologic symptoms, the most frequent complaint was ear itching in three patients (60%), followed by tinnitus, hearing loss and ear fullness in two (40%). The changes more often found during the physical examination were pinna oedema and opacity of the tympanic membrane. The main nasosinus symptoms were: presence of nasal obstruction, rhinorrhea and sneezing, reported by two patients (40%), and coryza, mucosal oedema, pale mucosa, granulation of the turbinates and turbinate hypertrophy were the primary findings. As to laryngeal complaints, cough, foreign body sensation, raucousness and choking were present in two cases (40%). The changes found on physical examination were inter-arytenoidal oedema, paresis of vocal folds and laryngeal hyperaemia (Table 2).

3 – Sjögren's syndrome (n = 5)

For patients with SS, tinnitus and ear fullness were present in three and four of the five patients, respectively; the most frequent changes were in conductive hearing loss and presence of a large amount of desquamation in the external auditory canal. Nasal obstruction was present in all patients. In the rhinoscopic examination, hyperaemia and oedema of mucosa were the observed findings. Dysphonia and raucousness were the only reported laryngeal symptoms; and the signs found were salivary gland hypertrophy, dry mouth and inter-arytenoidal oedema (Table 3).

Table 1 – Presence of otological signs and symptoms

	Wegener's granulomatosis n = 17	Relapsing Polychondritis n = 5	Syndrome of Sjögren n = 5	Systemic Lupus Erythematosus n = 3	Syndrome of Churg-Strauss n = 2
Otalgia	8 (47%)	1 (20%)	0	0	0
Otorrhea	4 (23%)	0	1 (20%)	0	0
Tinnitus	7 (41%)	2 (40%)	3 (60%)	1 (33%)	1 (50%)
Ear fullness	3 (18%)	2 (40%)	4 (80%)	0	1 (50%)
Hearing loss	9 (53%)	2 (40%)	2 (40%)	1 (33%)	1 (50%)
Hyperacusis	0	0	0	0	0
Ear pruritus	3 (18%)	3 (60%)	5 (100%)	0	0
Dizziness	1 (6%)	0	1 (20%)	0	0

Table 2 – Presence of nasal signs and symptoms

	Wegener's granulomatosis n = 17	Relapsing Polychondritis n = 5	Syndrome of Sjögren n = 5	Systemic Lupus Erythematosus n = 3	Syndrome of Churg-Strauss n = 2
Relapsing polychondritis	11 (65%)	2 (40%)	5 (100%)	1 (33%)	1 (50%)
Nasal obstruction	10 (59%)	2 (40%)	2 (40%)	1 (33%)	1 (50%)
Rhinorrhea	6 (35%)	0	4 (80%)	0	1 (50%)
Nasal itching	6 (35%)	0	2 (40%)	0	1 (50%)
Hyposmia	2 (12%)	0	0	0	0
Anosmia	1 (6%)	0	0	0	0
Cacosmia	5 (29%)	0	1 (20%)	0	1 (50%)
Postnasal drip	7 (41%)	2 (40%)	1 (20%)	0	2 (100%)

Table 3 – Aerodigestive pathways/pharyngeal symptoms

	Wegener's granulomatosis n = 17	Relapsing Polychondritis n = 5	Syndrome of Sjögren n = 5	Systemic Lupus Erythematosus n = 3	Syndrome of Churg-Strauss n = 2
Dysphonia	3 (14%)	1 (20%)	2 (40%)	2 (67%)	1 (50%)
Cough	4 (23%)	2 (40%)	0	0	1 (50%)
Snoring	0	0	0	0	0
Foreign body sensation	1 (6%)	2 (40%)	0	0	0
Dysphagia	0	0	0	0	0
Odynophagia	0	0	0	0	0
Dyspnea	6 (35%)	1 (20%)	0	1 (33%)	1 (50%)
Hemoptysis	1 (6%)	0	0	0	1 (50%)
Hawk	7 (41%)	2 (40%)	3 (60%)	0	1 (50%)
Heartburn	1 (6%)	1 (20%)	2 (40%)	0	0
Gagging	1 (6%)	2 (40%)	0	0	0

4 – Systemic Lupus Erythematosus (n = 3)

Among SLE patients, tinnitus and hearing loss were reported by one patient (33%), with presence of left ear sensorineural hearing loss and right ear conductive hearing loss. Among nasal symptoms, nasal obstruction and rhinorrhea were also present in one patient, and edema and coryza were the signs most often found. Dysphonia was present in two cases (67%), and the presence of glottic cleft during phonation and inter-arytenoidal oedema were the changes observed.

5 – Churg-Strauss syndrome (n = 2)

One patient (50%) with Churg-Strauss reported tinnitus, ear fullness and hearing loss, with conductive hearing loss at audiometry. At rhinoscopy, pale mucosa, turbinate hypertrophy and coryza were observed in patients. The complaints of dysphonia, cough, dyspnea, haemoptysis, and raucousness were compatible with the presence of oedema of laryngeal mucosa, glottic cleft and secretion, observed during the examination of the larynx.

In the evaluation of all the symptoms studied by region, all SS patients reported the presence of at least one otologic or nasal symptom, and also had audiometric change. Laryngeal symptoms were more frequent in patients with SLE, being present in two patients (66%) (Table 4); however, patients with SLE were those with fewer ear and nasal symptoms, or with

audiometric changes. These conditions were present in only one patient (33%) (Tables 5 and 6).

The audiometric changes (indicated in Table 6) found were described as sensorineural hearing loss (SNHL), conductive hearing loss (CHL) or mixed hearing loss (MHL). In the case of SNHL, the following distribution was observed: 29% of WG, 60% of PR, 20% of SJ, 33% of SLE and 0% of CSS. With MHL, no cases were observed. On the other hand, for CHL another distribution was observed: 23% of WG, 20% of PR, 80% of SJ, 33% of SLE and 50% of CSS.

Discussion

ENT manifestations in autoimmune diseases represent a diagnostic challenge for the rheumatologist, otolaryngologist and clinician.^{1,5,15,24,25} Generally, ENT symptoms may represent an early sign of an undiagnosed autoimmune disorder that often requires an immediate and aggressive immunosuppressive treatment.²⁵⁻²⁹ There are diseases of systemic action that present themselves with localized manifestations, and the region of the head and neck is an important site of these manifestations.⁵

Ear damage have been occasionally reported as a complication in the course of several rheumatic diseases.^{8,30} It is common, for example, to find sensorineural hearing loss with decreased hearing acuity or discrimination of sounds. Uni- or bilateral sensorineural hearing loss affecting medium and high frequencies have been reported in patients with SLE, and there is evidence of a strong association between hearing loss and

Table 4 – Other head and neck signs and symptoms

	Wegener's granulomatosis n = 17	Relapsing Polychondritis n = 5	Syndrome of Sjögren n = 5	Systemic Lupus Erythematosus n = 3	Syndrome of Churg-Strauss n = 2
Conjunctivitis	0	1 (20%)	2 (40%)	0	1 (50%)
Headache	3 (18%)	1 (20%)	0	0	1 (50%)
Facial paralysis	0	0	0	0	0

Table 5 – Findings of ENT physical examination

	Wegener's granulomatosis n = 17	Relapsing Polychondritis n = 5	Syndrome of Sjögren n = 5	Systemic Lupus Erythematosus n = 3	Syndrome of Churg-Strauss n = 2
Rhinology, change in	12 (70%)	3 (60%)	5 (100%)	1 (33%)	2 (100%)
Otoscopy, change in	7 (41%)	0	0	0	0
Nasofibroscopy, change in	7 (41%)	3 (60%)	4 (80%)	2 (67%)	2 (100%)
Otoscopy, change in	7 (41%)	2 (40%)	5 (100%)	1 (33%)	0

Table 6 – Otologic, nasal, and laryngeal symptoms and audiometric change in the studied diseases

	Otologic symptoms	Nasal symptoms	Laryngeal symptoms	Audiometric change
Wegener's Granulomatosis	9 (53%)	11 (65%)	7 (41%)	9 (53%)
Relapsing Polychondritis	3 (60%)	2 (40%)	2 (40%)	4 (80%)
Sjögren's Syndrome	5 (100%)	5 (100%)	3 (60%)	5 (100%)
Systemic Lupus Erythematosus	1 (33%)	1 (33%)	2 (67%)	1 (33%)
Churg-Strauss Syndrome	1 (50%)	2 (100%)	1 (50%)	1 (50%)

elevated titres of anticardiolipin antibodies. A sensorineural hearing loss in the course of Sjögren's syndrome (SS) is partly attributed to the presence of high titres of those antibodies.⁴ A sudden or gradual hearing loss may occur in about 50% of patients with recidivant polychondritis, and both in these as in patients with WG, a conductive hearing loss is the main otologic damage. According to literature, audiovestibular deficits are uncommon in patients with CSS.⁴ According to the findings of this trial, ear manifestations in the patients studied confirm the literature data, maintaining statistical similarity.

In literature we find data on vestibulocochlear system involvement by vascular lesions in the internal auditory artery, causing sensorineural dysacusis in addition to symptoms such as dizziness and tinnitus. According to the authors, the little mention of vestibular symptoms is due to the fact that the gradual involvement of the vestibular system promotes labyrinthine compensation.³¹

Laryngeal involvement is extremely rare and the symptoms can range from hoarseness to respiratory distress.³² Smith et al. published two cases with cricoarytenoid ulceration, stenosis and oedema. Kraus and Guerra-Bautista published a case with complete vocal fold paralysis in 1990. Tietel et al. published, in 1997, a review of cases of laryngeal involvement in SLE, in which laryngeal oedema occurred in 28% of cases and vocal paralysis in 11%.³²

Allergic rhinitis is often present in patients with Churg-Strauss syndrome.⁴ Symptoms such as nasal itching, airflow obstruction, coryza and recurrent sinusitis are common manifestations in CSS, GW and PR.^{9,33} In general, Churg-Strauss

syndrome is characterized by asthma, eosinophilia, and extravascular eosinophilic granulomata. Also, as part of the clinical manifestations of CSS, the first phase of this syndrome is characterized by asthma possibly associated with allergic rhinitis, and often complicated by nasal polyposis and recurrent rhinosinusitis.⁹ The other phases are manifestations of eosinophilia and/or eosinophilic infiltrates in the tissues (lungs, gastrointestinal tract) or of systemic vasculitis.

In the available literature, three stages of the natural history of CSS are described: (1) prodromal stage, characterized by asthma and allergy for several years, (2) eosinophilic stage with peripheral blood eosinophilia and an organic infiltrate that can decrease or increase over several years, and (3) systemic vasculitis stage, that can be life threatening.³⁰ Still, the main feature of ENT manifestations in this disease is an allergic rhinitis associated with nasal polyposis.^{30,33} According to Bacciu et al., allergic rhinitis is present in 42.8% of CSS patients studied.⁹

According to literature, in patients with GW, the respiratory tract is involved in 70-100% of cases, with nasal and paranasal involvement in 80-90% of cases.^{4,25,33,34} Chronic nasal obstruction with a clear rhinorrhea, nasal ulceration and oedema of the mucosa, besides perforation, erosion of the vomer and nasal deformity with "saddle nose" are classic signs of the disease. We can also observe cases of chronic secretory otitis media and tympanic membrane perforation, in addition to the cases described of sensorineural dysacusis, vertigo and tinnitus.^{4,25,33,34} The prevalence of otologic involvement is around 35%, being related to vasculitis and blockage of the

Eustachian tube due to the involvement of nasopharynx.^{4,25,33,34} Facial palsy is found in 8-10% of cases and results from vasculitis of facial nerve *vasa-vasorum*, granulomatous invasion of middle ear tissue, primary granulomatous lesion of the nerve, or a combination of these factors.^{4,25,33,34} Dysphonia, larynx stridor, wheezing, oral ulceration and oedema and gingivitis complement the picture of ENT manifestations.^{4,25,33,34}

It is also worth remembering the important complications and cardiovascular events in SLE, with risk of fatal complications.³⁵ In a transversal trial conducted at Hospital Universitário Barros Barreto (HUJBB/UFPB) during 1997-2006, the main complication in SLE patients was the infectious syndrome (76.4%), followed by renal (33.8%) and thromboembolic (4.2%) events.³⁶ The main sites of infection were pleura and lungs (45.4%). The middle ear infection represented 1.8% of the cases.³⁶ On the other hand, as a well-documented complication, we can find nasal septum perforation (which can manifest with nasal obstruction, epistaxis, posterior nasal discharge or crust formation into the nasal cavity), being attributed to local inflammation or ischemia.¹ Upper airway obstruction due to laryngeal involvement is a rare, but well documented, complication of SLE, which usually occurs in association with other signs and symptoms that indicate active disease.¹

Data from the literature show auricular chondritis as the most frequent and characteristic finding of the disease, present in 85% of cases, and in 40% of them as the initial manifestation.⁸ This condition may be uni- or bilateral, causing phlogistic signs, with swelling of the external ear canal, and that may lead to conductive hearing loss. Vasculitis of the internal auditory artery may cause cochlear and/or vestibular involvement by cochlear infarct or ischemia, resulting in sensorineural dysacusis.⁸ Moreover, among the seven diagnostic criteria established by McAdam et al., four of them involve the presence of symptoms that affect the upper respiratory tract or vestibulocochlear system.³⁷

Nasal compromise, arising from nasal chondritis, can result in a "saddle nose" in up to 50% of patients. The diagnosis of laryngo-tracheo-bronchial chondritis is also crucial due to its high morbidity and mortality.⁸

Xerostomia is a common feature of Sjögren's syndrome, being usual in patients with primary and secondary syndrome.³⁸ It is the most obvious symptom of this syndrome.³⁶ Patients often exhibit dryness of lips, tongue and pharynx and consequent painful burning sensation and of mucosa, accompanied by speech, chewing, swallowing and digesting food difficulty.³² More than one third of patients present systemic manifestations that can include vasculitis, cryoglobulinemia, autoimmune hepatitis, pulmonary fibrosis, central nervous system involvement, renal tubular acidosis, B-cell lymphomas and multiple myeloma.³³

Other trials showed oral symptoms of dry mouth in 86% and eye symptoms in 53% of patients.³⁹ In the same trial, 46% of patients exhibited ocular involvement, demonstrated by Schirmer test or by Rose Bengal staining; and in 85.7% of studied cases an involvement of the salivary gland (by scintigraphy, sialography or sialometry) was evidenced.³⁹ The literature review shows that the most obvious oral symptom is xerostomia, with dryness of lips, tongue and pharynx and with chewing, swallowing and speech difficulty, as well

as increased susceptibility to dental caries and periodontal disease.³⁶ About a third to half of patients display an usually symmetrical and recurrent parotid gland hypertrophy.⁴⁰

Finally, we must consider the large time lag between complaints of rheumatology patients and the correct diagnosis, already described. The vasculitis involving the airways, for example, is a common presentation of a vascular disease involving ANCA (anti-neutrophil cytoplasmic antibody) and can precede by several years the diagnosis of the disease.³³

One should keep in mind that the referral of patients for this trial occurred unevenly among specific rheumatology outpatient clinics, according to the aforementioned rheumatologic diseases; then, the patients' distribution does not represent the overall distribution of patients with rheumatic diseases.

Conclusion

This trial demonstrated the various ENT manifestations of a group of patients with rheumatologic diseases that commonly can be related to rheumatic diseases, according to other trials. The early identification of these symptoms as a manifestation of such diseases, both by the otolaryngologist as by the rheumatologist, is critical to the early implementation of an immunosuppressive treatment, thereby reducing the morbidity and mortality of these conditions.

Conflicts of interest

The authors declare no conflicts of interest.

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